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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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05/15/2007

Hans-Georg Frank

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EXAMINER

WOODWARD, CHERIE MICHELLE

ART UNIT

PAPER NUMBER

1647

MAIL DATE

DELIVERY MODE

10/16/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/575,864	Applicant(s) FRANK ET AL.	
	Examiner Cherie M. Woodward	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 5/21/2008, 9/8/2008, and 7/13/2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-35 is/are pending in the application.
- 4a) Of the above claim(s) 6-10, 16-26 and 28-35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 11-15, and 27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 17 April 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/11/2006</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 1-25, 27, 29, and 31), Formula 1(a), a peptidic compound that binds the IL-2R, structure (a), and SEQ ID NO: 1, in the replies filed on 4/21/2008, 9/8/2008, and 7/13/2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 6-10, 16-26, and 28-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 1-5, 11-15, and 27 are under examination as they are drawn to Formula 1(a), a peptidic compound that binds the IL-2R, structure (a), and SEQ ID NO: 1.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on 5/11/2006 has been considered by the examiner. A signed copy is attached hereto.

Advisory Notice

Specification

3. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification - Objections

4. The disclosure is objected to because of the following informalities: there are sequences listed in the specification without corresponding sequence identifiers. All sequences in the specification over four (4) amino acids long and over nine (9) nucleic acids long are required to be identified by a SEQ ID NO. Appropriate correction is required.

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Oath/Declaration - Defective

5. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because there are non-initialed and/or non-dated alterations have been made to the oath or declaration by inventor Rybka. See 37 CFR 1.52(c). A new oath is required.

Claim Rejections - 35 USC § 112, First Paragraph

Scope of Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-5, 11-15, and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific covalent bridge constructs linked to specific individual helix regions, in the specification examples and the specific embodiments known in the art, does not reasonably provide enablement for the claimed genus of generic covalent bridge constructs and non specific helix regions of individual peptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability, 5) existence of working samples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claims are drawn to a broad species of peptidic compounds having covalently closed bridge structures which branch off from suitable amino acid side chains of a peptide with alpha-helical conformation. In essence, the invention is drawn to specific peptide bridge structures of Formula 1(a), a peptidic compound that binds the IL-2R, structure (a), and SEQ ID NO: 1, as elected.

The narrow scope of the enabled claims, that only the structures in the instant Examples are enabled, is required in light of the teachings in the specification that these constrained bridges are "custom

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designed" and the teachings in the art that the construction of stabilizing bridges is highly unpredictable because of the different positions of attachment of the bridge on the amino acid structure of a helix of any given peptide, the stereochemistry, and cross-linker length (Schafmeister et al., J Am Chem Soc. 2000;122:5891-5892; at p. 5891, column 1, second paragraph). Because the instant claims are drawn to a genus of generic peptides having covalently closed bridge structures and because the specification and the art teach that each of the bridge structures must be specifically designed for each specific helix region of each individual peptide, it would require undue experimentation to make and use the invention as claimed.

Schafmeister et al., teach that peptides that bind macromolecular receptors in an extended conformation can often be converted to mimetics that retain binding but have improved protease resistance and membrane permeability (p. 5891, column 1, first paragraph). However, peptides that must fold upon themselves in order to bind a receptor have proven difficult to improve by similar approaches because of their larger size and the difficulty of mimicking functionality presented on a complex folded molecular surface (p. 5891, column 1, first paragraph). Schafmeister et al., teach that most peptides that bind their receptors in an alpha-helical conformation have little helical structure when free in solution. Thus, stabilizing the helical form of peptides is highly desired because stabilizing the helical form is expected to favor receptor binding. The helix formation reduces exposure of the polar amide backbone thereby reducing the barrier to membrane penetration and increasing the resistance to protease cleavage (p. 5891, column 1, first paragraph). Additionally, Schafmeister et al., teach that a number of approaches for covalent helix-stabilization have been reported including cross-links that are both polar and pharmacologically labile, such as disulfides, lactam bridges, olefinic cross-linking of the helices, and all-hydrocarbon cross-linking (also known as "peptide stapling") (p. 5891, column 1, second paragraph). Schafmeister et al., teach that the construction of these stabilizing bridges is highly unpredictable because of the different positions of attachment of the bridge on the amino acid structure of the helix, the stereochemistry, and cross-linker length (p. 5891, column 1, second paragraph). Some configurations impart significant stability and others actually destabilize the helix (p. 5891, column 1, second paragraph). Moreover, the actual structure of the cross-links positioned on one face of an alpha-helix is very dependent on the stereochemistry at the attachment points (p. 5891, column 1, third paragraph). Schafmeister et al., also teach that the bridges (or "peptide staples") are incorporated into the peptide at $i + 4$ or $i + 7$ positions and then connected to cross-link one or two turns of the helix (Figure 1 and p. 5891, column 2, first paragraph). See also, Braisted et al., US 20020151473 (17 October 2002).

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Applicants' claims are excessively broad due, in part, to the large genus of claimed peptidic compounds having covalently closed bridge structures. Broad claims may be rejected merely because they read on a significant number of inoperative species when examiner sets forth reasonable grounds in support of his or her conclusions that the claims may read upon inoperative subject matter and it becomes incumbent upon applicant either to reasonably limit claims to approximate area where operativeness has not been challenged or to rebut examiner's challenge by submission of representative evidence or by persuasive arguments based on known laws of physics and chemistry (see *In re Cook and Merigold*, 169 USPQ 298 (CCPA 1971)).

In the instant case, Examples 1-8 and 13 teach a specific amino acid peptide sequence structure for the IL-2 receptor to which a variety of bridge structures are attached. However, both the specification and the art disclose that each of the bridge structures must be specifically designed for each specific helix region of each individual peptide and that they cannot be constructed in a generic manner. Accordingly, Applicant is enabled for the specific covalent bridge structures taught as they are linked to specific helix regions of individual peptides, but Applicant is not enabled for a generic genus of bridge structures or for generic bridging to generic regions of helical peptides.

Additionally, in claim 12, the phrase "another part of the overall helical structure" is not supported given the requirement in the art and in the specification that the bridge structures must be specifically designed for each specific helix region of each individual peptide. The "another part" is inadequate guidance as to where the bridge structure is to be covalently bonded.

Claim 13 is not adequately supported by the specification and one of ordinary skill in the art would not know the structure of the peptide sequence if "at least one amino acid of the peptide sequence is replaced..." Without knowing which amino acid(s) is/are to be replaced and what they are being replaced with, the skilled artisan would be required to engage in undue experimentation. Claim 13 is nothing more than an invitation to experiment to determine a bridge structure will work with any given amino acid or other physiochemical substitution.

Claim 14 is not enabled for the generic genus of "freely chosen appropriate organic moieties." One of ordinary skill in the art would not know where to begin to "freely choose" an "appropriate organic moiety" without sufficient guidance from the specification. The phrase is an invitation for further experimentation.

Claim 15 is not enabled for pharmaceutical compositions. When the term "pharmaceutical" is used in the preamble of a claim, its intended use as a pharmaceutical must be shown. The intended use of the claim as a pharmaceutical is imputed to mean every intended use, including use as a therapeutic or a

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preventative. The claim, as written, fails to adequately limit any such intended use. Instead the claim generically requires use is in humans or animals to act as a functional IL-2 antagonist. The action of a functional IL-2 antagonist does not treat or prevent any disorder. Applicant appears to be speculating that the composition may work to antagonize IL-2, but there are no data showing use of any species of the claimed composition used in any pharmaceutical therapeutic or preventive regime. Further, the specification does not reasonably provide enablement any pharmaceutical use of the claimed genus of peptidic compositions for the treatment or prevention of any disorder. Without guidance from the specification, the skilled artisan cannot envision the treatment or prevention of any disease by administration of the claimed pharmaceutical composition by any means. For purposes of enablement, the specification must provide reasonable detail in order for those skilled in the art to carry out the invention. The teachings of the specification do not enabled a person of ordinary skill in the art to make and use the claimed pharmaceutical composition. Moreover, “[p]atent protection is granted only in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable.” *Genentech Inc. v. Novo Nordisk A/S*, 108 F.3d at 1366, 42 USPQ2d at 1005 (Fed. Cir.), cert. denied, 118 S. Ct. 397 (1997), (“Tossing out the mere germ of an idea does not constitute an enabling disclosure”).

The determination of whether Applicant has met his burden of disclosing how to make and use the invention to the public in order to satisfy the *quid pro quo* requirement of disclosure in exchange for a patent has not been adequately met by the instant claims or specification. From the early days of the republic, our patent law has required that in exchange for a government-sanctioned monopoly on the rights to an invention or discovery, the inventor must teach the world the secret behind the method or device. Compare 35 USC § 112 (1984) with Act of April 10, 1790, ch. 7, § 2, 1 Stat. 109 (“specification shall be so particular . . . as not only to distinguish the invention or discovery from other things before known and used, but also to enable a workman or other person skilled in the art of manufacture . . . to make, construct or use the same, to the end that the public may have the full benefit thereof, after the expiration of the patent term”); see also, *Bonito Boats, Inc. v. Thunder Craft Boats, Inc.*, 489 U.S. 141, 146-51, 103 L. Ed. 2d 118, 109 S. Ct. 971 (1989); *In re Goodman*, 11 F.3d 1046, 1050 (Fed. Cir. 1993) (specification must teach how to make and use the invention as broadly as it is claimed). The rationale for the enablement requirement is that an inventor deprives the public of nothing which it enjoyed before his discovery, but gives something of value to the community by adding to the sum of human knowledge. He may keep his invention secret and reap its fruits indefinitely. In consideration of its disclosure and the consequent benefit to the community, the patent is granted. *United States v. Dubilier Condenser Corp.*,

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289 U.S. 178, 186-87, 77 L. Ed. 1114, 53 S. Ct. 554 (1933) (citations omitted); see also *O'Reilly v. Morse*, 56 U.S. 62, 119-20, 14 L. Ed. 601, (15 How. 62, 127-28) (1853) (Taney, C.J.) (one skilled in the art must be able to produce precisely the described result by using the means specified by the inventor); *Grant v. Raymond*, 31 U.S. 217, 247 (31 Peters 141, 160) (1832) (Marshall, C.J.) (correct specification is a prerequisite to obtaining a patent in order to give the public "the advantage for which the privilege is allowed, and is the foundation of the power to issue the patent."). When a putative inventor fails or refuses to fulfill the obligation to teach precisely what is claimed, the inventor is not entitled to the protections of the patent law. See, e.g., *Morton Int'l, Inc. v. Cardinal Chem. Co.*, 5 F.3d 1464, 1469-70 (Fed. Cir. 1993) (affirming determination of lack of enablement where fifty examples in specification "obviously teach something," but not what was defined in the claims).

Claim Rejections - 35 USC § 112, First Paragraph

Written Description

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-5, 11-15, and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. This is a written description rejection, rather than an enablement rejection under 35 U.S.C. 112, first paragraph. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 19 USPQ2d 1111, (Fed. Cir. 1991), states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention, for purposes of the written description inquiry, is whatever is now claimed (see page 1117). A review of the language of the claim indicates that these claims are drawn to a genus, i.e., generic peptidic compounds having stabilizing bridges at i and i+7.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing characteristics of the genus. The factors to be

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considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). In *Regents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that, while applicants are not required to disclose every species encompassed by a genus, the description of the genus is achieved by the recitation of a representative number of species falling within the scope of the claimed genus. At section B(1), the court states, “An adequate written description of a DNA ... requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention.”

The instant claims are drawn to a genus of generic alpha-helical peptides having covalently closed bridge structures (i.e. peptide staples). There is a single species of the claimed genus disclosed that is within the scope of the claimed genus, i.e. structure (a) on SEQ ID NO: 1. The disclosure of a single disclosed species may provide an adequate written description of a genus when the species disclosed is representative of the genus. However, the present claim encompasses numerous species that are not further described. Additionally, the specification and the art disclose that each of the bridge structures must be specifically designed for each specific helix region of each individual peptide and that they cannot be constructed in a generic manner. There is no evidence that Applicant was in possession of a sufficient number of specific bridge structures designed for each specific helix region of individual peptides to support a description of the claimed genus. While “examples explicitly covering the full scope of the claim language” typically will not be required, a sufficient number of representative species must be included to “demonstrate that the patentee possessed the full scope of the [claimed] invention.” *Lizardtech v. Earth Resource Mapping, Inc.*, 424 F.3d 1336, 1345, 76 USPQ2d 1724, 1732 (Fed. Cir. 2005).

In the absence of sufficient recitation of distinguishing characteristics, the specification does not provide adequate written description of the claimed genus of generic peptidic compounds having stabilizing bridges at i and $i+7$. One of skill in the art would not recognize from the disclosure that the

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applicant was in possession of the genus. Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features (see, *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1895 (Fed. Cir. 2004); accord *Ex Parte Kubin*, 2007-0819, BPAI 31 May 2007, opinion at p. 16, paragraph 1). The specification does not clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed (see *Vas-Cath* at page 1116).

The concerns raised by the examiner specifically relate to aspects of Applicant's generic invention which are not adequately described. Applicant is encouraged to review the recent decision in *Carnegie Mellon University et al., v. Hoffman-La Roche, Inc., et al.*, Slip Op. 2007-1266 (Fed. Cir., 8 September 2008), where the CAFC specifically addressed the issue of generic claims to biological subject matter. The Court stated that "[t]he basic function of a patent specification is to disclose an invention. It has long been the case that a patentee 'can lawfully claim only what he has invented and described, and if he claims more his patent is void'" (citing *O'Reilly v. Morse*, 56 US (15 How.) 62, 121 (1853)) (Slip Op., at 10). "The written description serves a *quid pro quo* function 'in which the public is given 'meaningful disclosure in exchange for being excluded from practicing the invention for a limited period of time'" (citing *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 69 USPQ2d 1886 (Fed. Cir. 2004), quoting *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 970 (Fed. Cir. 2002) (Slip Op., at 10). The *Carnegie Mellon* Court held that "[o]ne must show that one has possession, as described in the application, of sufficient species to show that he or she invented and disclosed the totality of the genus" (Slip Op., at 18).

Applicant is referred to *Ariad Pharmaceuticals Inc. et al., v. Eli Lilly and Co.*, Slip Op. 2008-1248 (Fed. Cir. 3 April 2009), especially at p.7, stating that "the written description requirement is not satisfied by the appearance of mere indistinct words in a specification or a claim, even an original claim...A description of what a material does, rather than of what it is, usually does not suffice" quoting *Enzo Biochem Inc., v. Gen-Probe Inc.*, 323 F. 3d 956, 968 (citing *Regents of the Univ. of Cal. v. Eli Lilly*, 119 F.3d 1159, 1568 (Fed. Cir. 1997) and *Univ. of Rochester v. G.D. Searle & Co*, 358 F3d. 916, 926 (Fed. Cir. 2005). In *Ariad*, the Court held that to satisfy the written description requirement for the asserted claims, the specification must demonstrate that Applicant possessed the claimed methods by sufficiently disclosing the structure of the molecules capable of performing the disclosed function, citing *Capon v. Eshhar*, 418 F.3d 1349,1357 (Fed. Cir. 2005) (*Ariad*, Slip Op. at 10).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Jackson (J Am Chem Soc. 1991. 113:9391-9392) (cited in Applicant's IDS of 5/11/2006).

Jackson discloses cyclic peptides containing the following sequence: X-K-A-A-A-A-K-X wherein "X" represents 2-amino-6-mercaptohexanoic acid, and wherein the thiol groups are bonded together in disulfide linkage. It is noted that instant claim 1 recites that the carbon or nitrogen atoms may be shared with the side chain atoms of amino acids i and i+7, consists of one or two peptide bonds and one disulfide bridge. Stabilizing at i and i+4 is taught in the abstract.

12. Claims 1-5 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Phelan (J Am Chem Soc. 22 Jan 1997;119(3):455-460) (cited in Applicant's IDS of 5/11/2006).

Phelan et al., teach cyclic peptides with tethered glutamine residues at the I and i+7 positions (abstract). Lactamization between i and i+3 and i and i+4 is also taught at pp. 456 and 458 (see also, Figure 4 and Tables 2 and 3). N-terminal acetylation and C-terminal amidation of the peptides is disclosed at Figures 1 and 2 (p. 457).

13. Claims 1-5 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by (Schafmeister et al., J Am Chem Soc. 2000;122:5891-5892).

Schafmeister et al., teach that peptides that bind macromolecular receptors in an extended conformation can often be converted to mimetics that retain binding but have improved protease resistance and membrane permeability (p. 5891, column 1, first paragraph). However, peptides that must fold upon themselves in order to bind a receptor have proven difficult to improve by similar approaches because of their larger size and the difficulty of mimicking functionality presented on a complex folded molecular surface (p. 5891, column 1, first paragraph). Schafmeister et al., teach that most peptides that bind their receptors in an alpha-helical conformation have little helical structure when free in solution. Thus, stabilizing the helical form of peptides is highly desired because stabilizing the helical form is expected to favor receptor binding. The helix formation reduces exposure of the polar amide backbone

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thereby reducing the barrier to membrane penetration and increasing the resistance to protease cleavage (p. 5891, column 1, first paragraph). Additionally, Schafmeister et al., teach that a number of approaches for covalent helix-stabilization have been reported including cross-links that are both polar and pharmacologically labile, such as disulfides, lactam bridges, olefinic cross-linking of the helices, and all-hydrocarbon cross-linking (also known as “peptide stapling”) (p. 5891, column 1, second paragraph). Schafmeister et al., teach that the construction of these stabilizing bridges is highly unpredictable because of the different positions of attachment of the bridge on the amino acid structure of the helix, the stereochemistry, and cross-linker length (p. 5891, column 1, second paragraph). Some configurations impart significant stability and others actually destabilize the helix (p. 5891, column 1, second paragraph). Moreover, the actual structure of the cross-links positioned on one face of an alpha-helix is very dependent on the stereochemistry at the attachment points (p. 5891, column 1, third paragraph). Schafmeister et al., also teach that the bridges (or “peptide staples”) are incorporated into the peptide at $i + 4$ or $i + 7$ positions and then connected to cross-link one or two turns of the helix (Figure 1 and p. 5891, column 2, first paragraph). N-terminal acetylation and C-terminal amidation of the peptides is disclosed at p. 5892 (see footnote (10)).

Obviousness-Type Double Patenting Rejection

14. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or

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claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

15. Claim 1 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11/389,667. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same or overlapping subject matter. Claim 1 of the '667 application is drawn to a binding molecule comprising a support structure of at least one cyclic molecular subunit and at least two side chain subunits, characterized in that the side chain subunits are polypeptide chains consisting of natural and/or unnatural D- and/or L-amino acids and/or polynucleotide chains and the side chain subunits are covalently bonded to the support structure (compare instant claim 1). Instant claim 1 is drawn to peptidic compounds having covalently closed bridge structures wherein the bridge backbone, including the side chain atoms of amino acids i and $i+7$ of the peptide consists of one or two amide (peptide) bonds, one disulfide bridge and further 7-11, preferably 9 C- or N-atoms. Instant claim 4 The '667 specification states that the cyclic peptide structure "does not exclude that the binding molecules of the invention also contain disulfide bridges in addition to a more stable cyclic molecular subunit of the support structure (p. 5, last paragraph). "Such additional disulfide bonds will preferably be located at sites relatively distant from the support structure and will be introduced to stabilize a specific sterical configuration within and/or between two or more side chains" (p. 5, last sentence to p. 6, first sentence). The peptidic compounds of instant claim 1 overlap with the binding molecules of claim 1 of the '667 application, based on the claims themselves and the preferred embodiments set forth in the '667 specification. Applicant is reminded that MPEP § 804 (II) states, "When considering whether the invention defined in a claim of an application would have been an obvious variation of the invention defined in the claim of a patent, the disclosure of the patent may not be used as prior art. *General Foods Corp. v. Studiengesellschaft Kohle mbH*, 972 F.2d 1272, 1279, 23 USPQ2d 1839, 1846 (Fed. Cir. 1992). This does not mean that one is precluded from all use of the patent disclosure." (Emphasis added). "Further, those portions of the specification which provide support for the patent claims may also be examined and considered when addressing the issue of whether a claim in the application defines an obvious variation of an invention claimed in the patent. *In re Vogel*, 422 F.2d 438, 441-42, 164 USPQ 619, 622 (CCPA 1970)."

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

16. The prior art made of record and not presently relied upon is considered pertinent to applicant's disclosure:

- a. Braisted et al., US 20020151473 (17 October 2002).

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHERIE M. WOODWARD whose telephone number is (571)272-3329. The examiner can normally be reached on Monday - Friday 9:30am-6:00pm (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Cherie M. Woodward/
Primary Examiner, Art Unit 1647